REMARKS

The presently claimed invention features methods for identifying compounds that are candidate modulators of the drug resistance of an eukaryotic cell.

Rejections Under 35 U.S.C. §112, first paragraph

The Examiner rejected claims 1-4 as allegedly not enabled. The Examiner stated that, while the specification is enabling for "eukaryotic cells and known proteins and nucleic acid sequences encoding said proteins which modulate drug resistance in human cells", it is not enabling for "prokaryotic cells or mouse proteins obtained from the transplanted fibrosarcoma model and nucleic acid sequences encoding said proteins which do not have a known human homolog". The Examiner went on to state that undue experimentation would be required to practice the invention due to the lack of teachings regarding "assessing the effect of a test compound on drug resistance sequences in prokaryotic cells" and "the exact human sequences of semaphorin D or 24p3".

The specification describes studies on the expression of murine semaphorin, murine B94, murine mel-14, murine 24p3, murine proliferin, and murine maspin in drug resistant cancer cells. The specification also discloses the GenBank Accession Number for each of these murine genes as well as the GenBank Accession Number for the human homologs of semaphorin, murine B94, murine mel-14, murine 24p3, murine proliferin, and murine maspin (see, e.g., page 14, lines 24-35). The GenBank Accession Numbers disclosed for the murine genes and human homologs are summarized below.

Gene	**Murine GenBank Accession Number**	**Human GenBank Accession Number**
semaphorin	X85993	L26081
b94	L24118	M92357
mel-14	M25324	M25280
24p3	X81627	----------
proliferin	K03235	---------
maspin	U54705	U04313

The present claims are drawn to methods which entail determining the level of expression of certain gene in a "eukaryotic cell". In addition, the present claims are drawn to methods whtat entail "determining the level of expression of a gene encoding an mRNA comprising a nucleotide sequence selected from the group consisting of the nucleotide sequence of any of GenBank Accession Numbers X85993, L26081, L24118, M92357, M25324, M25280, X81627, K03235, U54705, and U04313". All of these GenBank Accession Numbers are disclosed in the specification. Moreover, the specification discloses methods for measuring expression of mRNA and proteins in eukaryotic cells (see, e.g., pages 39-45 of the specification). Thus, the specification enables one skilled in the art to perform the claims methods for identifying candidate modulators of the drug resistance of a eukaryotic cell. In view of the forgoing, Applicant respectfully requests that the rejections under 35 U.S.C. §112, first paragraph be withdrawn.

Rejections Under 35 U.S.C. §102

The Examiner rejected claims 1 and 4 as allegedly anticipated by Shyjan et al. (U.S. Patent 5,932,422).

The present claims entail a step of "determining the level of expression of a gene encoding an mRNA comprising a nucleotide sequence selected from the group consisting of the nucleotide sequence of any of GenBank Accession Numbers X85993, L26081, L24118, M92357, M25324, M25280, X81627, K03235, U54705, and U04313 in an eukaryotic cell." Nothing in Shyjan et al. teaches or suggests determining the level of expression of any of the genes specified in the presently pending claims. Thus, Shyjan et al. cannot anticipate any of the presently pending claims. In view of the forgoing, Applicant respectfully requests that that rejections under 35 U.S.C. §102 be withdrawn.

Rejections Under 35 U.S.C. §103

The Examiner rejected claims 1-4 as allegedly obvious in view of Nilsen-Hamilton et al. (*Gene* 51:163, 1987) in view of Stein (*Proc. Am. Assoc. Cancer Res.* 38:A3215, 1997). According to the Examiner, Nilsen-Hamilton et al. teach "multidrug resistance-associated protein, MRP, as the human homolog of mouse proliferin" and Stein et al. "teach the modulation

of MRP expression levels by TNF-alpha". The Examiner then concludes that it would have been obvious "to measure the modulation of the expression or activity or proliferin in the presence or absence of a test compound" motivated by "the teachings of Nilsen-Hamilton et al. on the homology between the proliferin gene and the MRP gene."

The Examiner's reasoning is flawed because it does not appear that the cited prior art teaches that the human multidrug resistance protein (MRP) gene of Stein et al. is the human homolog of murine proliferin. First, the full name of the protein called "MRP" by Nilsen-Hamilton et al. is "mitogen-regulated protein" not multidrug resistance protein. Second, the mitogen-regulated protein described by Nilsen-Hamilton et al. is a murine protein, not a human protein. For example, Nilsen-Hamilton et al. state that "[m]itogen-regulated protein is a glycoprotein secreted by Swiss murine 3T3 cells. Thus, it does not appear that the cited prior art teaches that the human MRP of Stein et al. is related to murine proliferin. Thus, the cited references cannot render any of the present claims obvious. In view of the forgoing, Applicant respectfully requests that the rejections under 35 U.S.C. §103 be withdrawn.

Conclusion

Attached is a marked-up version of the changes being made by the current amendment.

Applicant asks that all claims be allowed. Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

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Version with markings to show changes made

In the claims:

Claims 1-4 have been cancelled.